The value of autopsies in the era of high-tech medicine: discrepant findings persist

Chantal C H J Kuijpers,[1] Judith Fronczek,[1,2] Frank R W van de Goot,[1] Hans W M Niessen,[2,3,4] Paul J van Diest,[5] Mehdi Jiwa[1]

[1]Symbiant Pathology Expert Centre, Alkmaar, The Netherlands
[2]Department of Pathology, VU Medical Centre, Amsterdam, The Netherlands
[3]Department of Cardiac Surgery, VU Medical Centre, Amsterdam, The Netherlands
[4]ICaR-VU, VU Medical Centre, Amsterdam, the Netherlands
[5]Department of Pathology, University Medical Centre Utrecht, Utrecht, The Netherlands

Correspondence to
Dr Mehdi Jiwa, Department of Pathology, Alkmaar Medical Centre, Symbiant Pathology Expert Centre, PO Box 501, Alkmaar, Noord-Holland 1815 JD, The Netherlands; m.jiwa@symbiant.nl

CCHJK and JF contributed equally.

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ABSTRACT

Aims Although the autopsy is still the gold standard for quality assessment of clinical diagnoses, autopsy rates have been declining over the last decades to <10%. The aim of this study was to investigate the value of autopsies in the high-tech medicine era by determining the frequency of discrepancies between clinical and autopsy diagnoses.

Methods We classified all adult autopsy cases (n=460), performed at Symbiant, Pathology Expert Centre, in 2007 and 2012/2013, as having major, or minor discrepancy or total concordance. The roles of possible contributory factors were analysed. Finally, we assessed the role of microscopic examination in identifying cause of death.

Results Major and minor discrepancies were found in 23.5% and 32.6% of the classifiable autopsies, respectively. Most commonly observed major discrepancies were myocardial infarction, pulmonary embolism and pneumonia. Improper imaging and discontinuation of active treatment were significantly associated with a higher and a lower frequency of major discrepancies, respectively. Comparing 2007 and 2012/2013, the frequency of minor discrepancies significantly increased from 26.8% to 39.3%. Final admission length of >2 days was significantly associated with a lower frequency of class III minor discrepancies. Microscopic examination contributed to establishing cause of death in 19.6% of the cases.

Conclusions Discrepant findings persist at autopsy, even in the era of high-tech medicine. Therefore, autopsies still should serve as a very important part of quality control in clinical diagnosis and treatment. Learning from individual and system-related diagnostic errors can aid in improving patient safety.

INTRODUCTION

The autopsy is for long been regarded as the 'gold standard' as the most important tool for retrospective quality assessment of clinical diagnoses as well as a key educational tool.[1] This is evident from previous studies comparing clinical diagnoses and autopsy findings, which revealed major discrepancies in approximately 25% of the deceased patients that underwent postmortem examination.[2 3]

However, throughout the world, autopsy rates have been declining over the past few decades.[4–6] Reasons for this decline include the non-reimbursement of autopsies, clinicians' fear of medicolegal problems and advances in laboratory testing and imaging techniques that often result in the belief among clinicians that the autopsy had become redundant.

We assessed the value of autopsies by determining the major and minor discrepancy rates in a total of 460 consecutive autopsy cases, divided over two time periods. In the most recent time period, the majority of autopsies was performed by a specialised autopsy pathologist. Furthermore, we analysed the influence of several factors, including age, sex, length of final admission and the use of imaging techniques on the frequency of major and minor discrepancies. Finally, we determined the role of microscopic examination in identifying the cause of death (COD).

METHODS

Cases and data extraction

We retrospectively reviewed all consecutive adult (>18 years) autopsy cases, performed at the three locations of Symbiant, Pathology Expert Centre (Alkmaar Medical Centre, Zaandam Medical Centre and Westfriesgasthuis Hoorn) from 2007 and from 2012 on up to July 2013. Partial autopsies restricted to certain parts of the body (eg, brain, thorax) were excluded, as well as autopsies from other local hospitals whose patient charts were not available to us. Autopsies requested by general practitioners or other primary care providers were included, but analysed separately as 'external autopsies'. In 2007, all autopsies were performed by general pathologists. Starting from April 2011, three specialised autopsy pathologists performed the majority of the autopsies.

All clinical and postmortem diagnoses were recorded. Clinical diagnoses were extracted from the clinical information written on the autopsy request form and from patient charts including clinicians' letters directed to the general practitioner, the medical history and radiology results. Postmortem diagnoses were extracted from macroscopic and microscopic autopsy findings described in the autopsy report.

From every case, the following data were recorded: age, sex, length of final admission, whether imaging techniques (MRI, CT, PET, ultrasound and X-ray) were applied during life not more than 1 month before death, whether active treatment was discontinued, and the last admission unit. Furthermore, we recorded which pathologist performed the autopsy (autopsy pathologist vs general pathologist), whether the autopsy also included the brain, the postmortem time and the time until completion of the preliminary and the final autopsy report.

Imaging

We assessed all cases of patients who underwent imaging in the hospital of final admission not more

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than 1 month before death. For these patients, we determined whether it was possible to visualise the COD with imaging. If so, we determined whether imaging was applied to the proper part of the body (brain, thorax, abdomen, neck) needed to diagnose the COD and whether the proper imaging modality was used. For example, an X-ray in case of a pulmonary embolism was considered an improper imaging modality, as the proper imaging modality to diagnose a pulmonary embolism is a CT pulmonary angiography.[7]

Classification of discrepancies

We classified the discrepancies between clinical and postmortem diagnoses according to the Goldman classification system,[8] modified by Battle *et al*,[9] as described by Schwanda-Burger *et al*.[10] Major discrepancies (classes I and II) are missed diagnoses related to the COD. Knowledge before death would have changed management of care and could have prolonged survival or cured the patient (class I), or probably would not have changed the outcome (class II). Minor discrepancies (classes III or IV) are not directly related to the COD. Class III includes diseases with symptoms that should have been treated or that would ultimately have affected the prognosis. Class IV includes minor non-diagnosable diseases or events with possible epidemiological or genetic importance. Full concordance was classified as class V, and non-classifiable cases were assigned class VI. In case of two or more discrepant findings, the case was classified according to the most severe Goldman class.

All cases were classified by one specialised autopsy pathologist (JF). For the equivocal cases, a senior autopsy pathologist (FRWvdG) was consulted.

In case of insufficient clinical information, 'discrepant' findings were appointed non-classifiable (class VI). In cases where active treatment was withdrawn, we only classified discrepant diseases that certainly or most probably developed before active treatment discontinuation (eg, liver cirrhosis or neoplasms). Cases were designated class VI if the time point of origination of the discrepant disease was doubted (eg, pneumonia or myocardial infarction).

Role of microscopy

We analysed the role microscopic examination, of histochemical and immunohistochemical stainings, played in identifying COD. We determined whether histology contributed to establishing COD (ie, provided COD, changed COD or added to COD made by macroscopical examination), confirmed COD or played no role in determining COD. The same classification was used by Fronczek *et al*[11] in their study, determining the role of histology in forensic autopsies. Cases were non-classifiable if there was no clearly defined COD reported, if the report lacked either the diagnosis made at macroscopical or at microscopical examination, or if diagnoses made at macroscopical and microscopical examination were not reported separately.

Statistical analysis

Statistical analysis was performed with the SPSS statistics program (Windows V.20). χ^2 analysis was used to compare the frequencies of discrepancies between the two time periods. Furthermore, we performed logistic regression (OR, 95% CI and p value) for univariate (UV) and multivariate (MV) analysis. To make sure not to miss any possible contributory factor, all factors with a p value<0.2 in UV analysis were included in MV analysis. In MV analysis, p values<0.05 were considered statistically significant. A non-parametric median test was used to compare median times to autopsy report completion. All p values reported are two-sided.

RESULTS

Numbers

A total of 740 autopsies were performed. Autopsy rates decreased from 13.2% in 2007 to 6.6% in 2012/2013. Eventually, 460 autopsies were included in this study. The 280 excluded cases comprised 163 patients under the age of 18 (including foetuses), 108 patients from other local hospitals, 6 partial autopsies (3 brain autopsies, 2 thoracic autopsies and 1 liver autopsy) and 3 cases that were not signed out by the end of the inclusion period.

The included autopsies were divided into two groups, clinical and external autopsies, and analysed separately. Table 1 summarises the patient characteristics. The 'clinical autopsies' included 362 patients that were hospitalised or stayed at least 1 h at the emergency department. The 'external autopsies' included 98 cases submitted by a general practitioner, a nursing home physician or a forensic physician, or patients who had stayed at the emergency department for less than 1 h.

Discrepant autopsy findings

Table 2 illustrates the frequencies and percentages of Goldman classes in all autopsies (n=460), separately analysed for the two time periods. Overall, major discrepancies were observed in 18.1% of cases, minor discrepancies in 26.6% of cases and full concordance was observed in 37.8%. Comparing 2007 and 2012/2013, the frequency of major discrepancies decreased (from 20.1% to 16.0%; p=0.256), and the frequency of minor discrepancies significantly increased (from 21.8% to 31.2%; p=0.023). Furthermore, in total 17.6% of cases were non-classifiable, mostly due to insufficient clinical information, which was predominantly seen in the 'external autopsies' (57.1%). Cases where no clear COD had been found or one had not been specified in the report, or where active treatment was withdrawn also qualified as non-classifiable.

In the subgroup of clinical autopsies, 25/362 (6.9%) were non-classifiable. Table 3 shows the percentages of discrepancies in all 337 classifiable clinical autopsy cases (classes I–V), separately analysed for the two time periods. Overall, major discrepancies were found in 23.5%, minor discrepancies in 32.6% and full concordance was observed in 43.9%. Comparing 2007 and 2012/2013, the frequency of major discrepancies decreased (from 25.2% to 21.6%; p=0.434), and the frequency of minor discrepancies significantly increased (from 26.8% to 39.3%; p=0.015).

Tables 4 and 5 summarise clinical diagnosis (including differential diagnoses) and autopsy diagnoses of all class I and class II discrepant cases, respectively. The most commonly observed major discrepancies were myocardial infarction (n=18), pulmonary embolism (n=15) and pneumonia (n=11). Other common major discrepancies were malignancy (n=7), fungal infection (n=6), ruptured aneurysm, aortic dissection or aorta-oesophageal fistula (n=6), acute pancreatitis (n=5) and gastrointestinal perforation, severe bleeding or both (n=5).

The most commonly observed minor discrepancies were benign tumours (n=23), polyps (n=18), cysts (n=16), malignancies that were not contributory to the COD (n=15), gallbladder/kidney/prostate stones (n=11), diverticulosis (n=10), liver cirrhosis (n=9) and multinodular goitre (n=6).

Imaging

Imaging was performed not more than 1 month before death in 300/337 classifiable clinical autopsy cases (89.0%). In 29.7% of the cases, COD could not have been observed with imaging.

Table 1 Patient characteristics of the included autopsies

	Clinical autopsies		External autopsies	
	2007 (n=195)	2012/2013 (n=167)	2007 (n=34)	2012/2013 (n=64)
Age				
Average (SD)	71.8 (13.5)	72.2 (11.2)	57.8 (17.7)	59.5 (13.6)
Range	20–96	35–94	20–89	25–89
Sex				
Male	104 (53.3%)	95 (56.9%)	22 (64.7%)	48 (75.0%)
Female	91 (46.7%)	72 (43.1%)	12 (35.3%)	16 (25.0%)
Length of final admission (days)				
Average (SD)	9.4 (11.1)	9.3 (9.8)	–	–
Range	0–60	0–44	–	–
Imaging (within 1 month before death)				
Yes	176 (90.3%)	144 (86.2%)	1 (2.9%)	7 (10.9%)
No	19 (9.7%)	23 (13.8%)	7 (20.6%)	20 (31.1%)
Unknown	–	–	26 (76.5%)	37 (57.8%)
Active treatment discontinuation				
Yes	66 (33.8%)	80 (47.9%)	–	–
No	114 (58.5%)	71 (42.5%)	34 (100%)	64 (100%)
Unknown	15 (7.7%)	16 (9.6%)	–	–
Postmortem time (days)				
Average (SD)	1.1 (0.9)	0.9 (0.8)	1.28 (1.3)	1.39 (1.4)
Range	0–4	0–3	0–4	0–7
Pathologist that performed the autopsy				
General pathologist	195 (100%)	77 (46.1%)	34 (100%)	24 (37.5%)
Autopsy pathologist	–	90 (53.9%)	–	40 (62.5%)
Brain autopsy performed				
Yes	26 (13.3%)	38 (22.8%)	8 (23.5%)	21 (32.8%)
No	169 (86.7%)	129 (77.2%)	26 (76.5%)	43 (67.2%)
Last admission unit/origin of the patient				
Internal medicine	44 (22.6%)	51 (30.5%)	–	–
Intensive care	35 (17.9%)	38 (22.8%)	–	–
Surgery	33 (16.9%)	18 (10.8%)	–	–
Cardiology	25 (12.8%)	9 (5.4%)	–	–
Lung	21 (10.8%)	16 (9.6%)	–	–
Emergency department	21 (10.8%)	12 (7.2%)	7 (20.6%)	22 (34.4%)
Geriatrics	9 (4.6%)	5 (3.0%)	–	–
Neurology	5 (2.6%)	9 (5.4%)	–	–
Gastrointestinal	1 (0.5%)	7 (4.2%)	–	–
Orthopaedics	1 (0.5%)	1 (0.6%)	–	–
Plastic surgery	–	1 (0.6%)	–	–
General practitioner	–	–	25 (73.5%)	33 (51.6%)
Nursing home physician	–	–	2 (5.9%)	6 (9.4%)
Forensic physician	–	–	–	3 (4.7%)

Table 2 Goldman classification for the full group of autopsy cases evaluated for discrepancies between clinical and autopsy diagnoses (n=460), separately analysed for 2007 and 2012/2013

			2007			2012/2013		
		Total (%)	Frequency	Percentage		Frequency	Percentage	
Major	Class I	18.1	26	11.4	20.1	18	7.8	16.0
	Class II		20	8.7		19	8.2	
Minor	Class III	26.6	17	7.4	21.8	21	9.1	31.2
	Class IV		33	14.4		51	22.1	
	Class V	37.8	98	42.8		76	32.9	
	Class VI	17.6	35	15.3		46	19.9	
	Total		229			231		

Table 3 Goldman classification for the subgroup of classifiable (classes I–V) clinical autopsy cases (n=337) evaluated for discrepancies between clinical and autopsy diagnoses, separately analysed for 2007 and 2012/2013

			2007			2012/2013		
		Total (%)	Frequency	Percentage		Frequency	Percentage	
Major	Class I	23.5	25	14.0	25.2	17	10.8	21.6
	Class II		20	11.2		17	10.8	
Minor	Class III	32.6	16	8.9	26.8	17	10.8	39.3
	Class IV		32	17.9		45	28.5	
	Class V	43.9	86	48.0		62	39.2	
	Total		179			158		

Table 4 Comparison of clinical diagnoses (including differential diagnoses) and autopsy diagnoses of all class I major discrepant cases (n=42)

Clinical (differential) diagnoses	Autopsy diagnoses
1. Gastrointestinal haemorrhage	1. Ruptured aortic aneurysm
2. Cerebrovascular accident	2. Ruptured aortic aneurysm
3. Gastroenteritis	3. Gastrointestinal haemorrhage, duodenal ulcer
4. Sepsis	4. Endocarditis
5. Myocardial infarction, alcohol withdrawal syndrome	5. Acute necrotising pancreatitis
6. Subdural haematoma, myocardial infarction	6. Subdural haematoma, pulmonary embolism
7. Liver cirrhosis	7. Liver cirrhosis, myocardial infarction, pneumonia
8. Pancreas or liver malignancy, cholangitis, peritonitis	8. Perforated stomach lesion, gastrointestinal haemorrhage
9. Perforated duodenum	9. Pulmonary embolism
10. Non-Hodgkin's lymphoma, pneumonia	10. Pulmonary embolism
11. Metastatic breast carcinoma	11. Metastatic breast carcinoma, bilateral pneumonia
12. Liver cirrhosis, oesophageal varices, gastrointestinal haemorrhage	12. Liver fibrosis, oesophageal varices, gastrointestinal haemorrhage, bilateral pneumonia
13. Hypokalaemia-induced arrhythmia	13. Pneumonia
14. Malignancy, pulmonary embolism, cardiac decompensation	14. Cardiac tamponade, uremic pericarditis
15. Mors subita after toe surgery for osteomyelitis	15. Mechanical obstruction aortic valve, oesophageal carcinoma
16. Pneumonia, sepsis, diffuse intravasal coagulation	16. Diffuse intravasal coagulation, *Aspergillus* pneumonia
17. Metastatic frontal sinus carcinoma, pneumonia, pulmonary embolism	17. Metastatic undifferentiated carcinoma, *Candida albicans* pneumonia
18. Cardiac pathology, malignancy, parasitic infection	18. Pancreatitis, peritonitis
19. Metastatic breast carcinoma, myelodysplastic syndrome, intestinal ischaemia, perforated diverticulitis	19. Metastatic breast carcinoma, pulmonary embolism
20. Intestinal ischaemia	20. Intestinal ischaemia, pulmonary embolism
21. Cerebrovascular accident	21. Myocardial infarction, pleural empyema
22. Pneumonia, myocardial infarction, sepsis	22. Sepsis, pulmonary embolism
23. Blood loss after hip surgery	23. Ruptured aorta
24. Sepsis, cholecystitis, cardiac decompensation	24. Exsanguination from the wound bed of the gall bladder
25. Pneumonia, enterocolitis	25. Pneumonia, sepsis, acute cholecystitis with perforation
26. Sepsis, stomach and duodenal ulcer	26. Pulmonary embolism, *Aspergillus* pneumonia, intestinal ischaemia
27. Mediastinal undifferentiated tumour, sepsis, pleural empyema, arrhythmia, myocardial infarction	27. Hilar undifferentiated carcinoma, pulmonary embolism
28. Pancreatic carcinoma	28. Metastatic pancreatic carcinoma, pneumonia, pulmonary embolism
29. Sepsis, diverticulitis, endocarditis	29. Acute necrotising pancreatitis
30. Metastatic oesophageal carcinoma, pulmonary embolism, myocardial infarction, bowel perforation	30. Pneumonia
31. Acute coronary syndrome, myocardial infarction	31. Ruptured aortic aneurysm
32. Pulmonary embolism after breast lipofilling	32. Fat embolism
33. Sepsis, pneumonia, pleural empyema, pulmonary embolism	33. Metastatic lung carcinoma, pyogenic pericarditis
34. Salmonella sepsis, endocarditis	34. Endocarditis, colitis, acute pancreatitis, *Aspergillus* pneumonia
35. Sepsis	35. Pulmonary embolism
36. Blood loss of unknown origin	36. Exsanguination from aortoesophageal fistula
37. Urinary tract infection	37. Pulmonary embolism
38. Cardiac tamponade	38. Aortic dissection, myocardial infarction
39. Candida esophagitis	39. Pneumonia, sepsis
40. Arrhythmia	40. Lymphocytic myocarditis
41. Pneumonia, space occupying lesion lung	41. Lung adenocarcinoma, myocardial infarction, pulmonary embolism
42. Unexplained dyspnoea	42. *Aspergillus* pneumonia, pulmonary embolism, metastatic adenocarcinoma lung

Table 5 Comparison of clinical diagnoses (including differential diagnoses) and autopsy diagnoses of all class II major discrepant cases (n=37)

Clinical (differential) diagnoses	Autopsy diagnoses
1. Cardiac decompensation, pneumonia, unspecified infection	1. Myocardial infarction, pulmonary embolism, acute respiratory distress syndrome
2. Pneumonia	2. Malignant mesothelioma
3. Mors subita after hip replacement	3. Myocardial infarction
4. Metastatic lung carcinoma	4. Metastatic lung carcinoma, pneumonia
5. Pneumonia, amyloidosis	5. Pneumonia, lung adenocarcinoma
6. Mors subita after resection of sigmoid carcinoma. Metastases?	6. Myocardial infarction
7. Pneumonia, space occupying lesion intra-abdominal	7. Pneumonia, myocardial infarction
8. Unspecified infection, acute respiratory distress syndrome	8. Pneumonia, endocarditis
9. Cardiac decompensation	9. Myocardial infarction
10. Metastatic non-Hodgkin's lymphoma	10. Metastatic non-Hodgkin's lymphoma, myocardial infarction
11. Abdominal haematoma, endocarditis, morbus Kahler	11. Retroperitoneal haematoma, necrotising adenocarcinoma of the coecum with abscess formation
12. Resection double tumour colon, postoperative intestinal necrosis	12. Ischaemic small intestines, mesenteric vessel thrombosis
13. Acute pancreatitis, sepsis	13. Acute necrotising pancreatitis, sepsis, myocardial infarction
14. Pneumonia	14. Diffuse alveolar damage
15. Cardiac decompensation, urosepsis	15. Myocardial infarction
16. Mors subita after hip surgery	16. Myocardial infarction
17. Sepsis, myocardial infarction	17. Sepsis, bleeding from stomach ulcer
18. Lung carcinoma, retroperitoneal haematoma	18. Metastatic renal cell carcinoma
19. Meningitis	19. Subacute meningitis, pulmonary embolism
20. Sepsis, diffuse intravasal coagulation, lung haemorrhage	20. Sepsis, lung haemorrhage, bleeding from oesophageal varices
21. Sepsis	21. Peritonitis, perforation stomach ulcer
22. Pancreatic carcinoma, cholangitis, sepsis	22. Pancreatic carcinoma, bile duct adenocarcinoma
23. Duodenal ulcer, cardiac decompensation, cardiac arrest	23. Cardiac decompensation, vascular amyloidosis
24. Intestinal ischaemia, ruptured abdominal aortic aneurysm	24. Intestinal ischaemia, abdominal aortic aneurysm, hepatic infarction, arterial thrombosis (mesenteric, hepatic and pulmonary)
25. Space occupying lesion/malignancy right transsphenoidal orbit, cerebral infarction	25. Meningioma, cerebral infarction, thrombosis carotid artery with *Aspergillus* infection
26. Sepsis, metastatic tumour of unknown origin	26. Sepsis, metastatic endometrial carcinoma, endocarditis, pancreatitis
27. Breast carcinoma, pulmonary embolism, myocardial infarction	27. Breast adenocarcinoma, pulmonary embolism, lymphocytic myocarditis
28. Cardiac decompensation, malignancy	28. Cardiac decompensation, airway infection
29. Metastatic adenocarcinoma of unknown origin, pneumonia	29. Metastatic non-small cell carcinoma lung, pneumonia, acute respiratory distress syndrome, herpes esophagitis
30. Bowel resection due to ischaemia, sepsis	30. Sepsis, *Aspergillus* pneumonia
31. Malignancy, peritonitis	31. Metastatic tumour of unknown origin, peritonitis, myocardial infarction
32. Cardiac decompensation, malignancy	32. Coronary artery thrombosis, myocardial infarction
33. Pneumonia, malignancy	33. Pneumonia, coronary artery thrombosis, myocardial infarction
34. Cardiac decompensation, endocarditis	34. Myocardial infarction
35. Most subita (myocardial infarction?) after bowel resection due to ischaemia	35. Intestinal ischaemia, cardiac ischaemia, peritonitis, pneumonia
36. Sepsis, arrhythmia, bleeding abdominal aortic aneurysm	36. Ruptured abdominal aortic aneurysm, myocardial infarction
37. (Metastatic) lung carcinoma	37. Metastatic non-small cell lung carcinoma, pneumonia

The proper imaging modality for the body part needed to determine the COD was applied in 50.7%. Imaging was performed on another body part or with a different imaging modality than needed in 5.3% and 10.3%, respectively.

Factors contributing to discrepancies

Tables 6 and 7 show analyses of possible contributory factors to major and minor discrepancies, respectively. The following factors contributed to major discrepancies in UV analysis: advanced age, sex (female>male), length of final admission >2 days, the use of an improper imaging modality or imaging of a different body part, no active treatment discontinuation, and no brain autopsy included. Factors that contributed to minor discrepancies were active treatment discontinuation, autopsy performed in 2012 or 2013 and autopsy performed by an autopsy pathologist. Because the factors time period and type of pathologist are statistically related, only the most significant factor (time period) was included in the MV analysis.

MV analysis showed that the use of an improper imaging modality or imaging of an improper body part was significantly associated with a higher percentage of major discrepancies. Furthermore, active treatment withdrawal significantly contributed to a lower frequency of major discrepancies and a higher frequency of minor discrepancies (based on adjusted OR). Additionally, longer admission length (>2 days) was significantly associated with a lower frequency of class III discrepancies (OR=0.433 (95% CI 0.197 to 0.948); p=0.036).

Role of microscopy in identifying COD

Table 8 shows that microscopic examination contributed to establishing COD in 19.6% of the cases, it confirmed macroscopical diagnoses in 47.8%, played no role in identifying COD in 16.5% and 16.1% of the cases were non-classifiable. Microscopic examination most commonly played a role in diagnosing pneumonia (n=28), myocardial infarction (n=11) and lymphocytic or catecholamine-induced myocarditis (n=10) as COD.

Table 6 Analysis of possible contributory factors to major discrepancies between clinical and final pathology diagnosis at autopsies

	UV analysis			MV analysis		
	OR	95% CI	p Value	OR	95% CI	p Value
Age	1.033	1.009 to 1.057	0.006*	1.022	0.996 to 1.048	0.098
Sex	1.607	0.968 to 2.668	0.067*	1.494	0.818 to 2.730	0.192
Length of final admission >2 days	1.497	0.850 to 2.637	0.162*	1.737	0.857 to 3.517	0.125
Imaging (y/n)	1.662	0.667 to 4.140	0.276			
Imaging						
Proper imaging	1.000					
No imaging	0.726	0.279 to 1.890	0.512	0.739	0.213 to 2.557	0.633
Improper imaging	3.594	1.799 to 7.181	<0.001*	2.851	1.299 to 6.255	0.009†
Not imagable	0.951	0.497 to 1.817	0.878	0.929	0.448 to 1.930	0.844
Active treatment discontinuation	0.479	0.265 to 0.866	0.015*	0.458	0.239 to 0.878	0.019†
Admission unit‡						
First aid	1.000		0.466			
Cardiology	1.833	0.576 to 5.831				
Surgery	1.061	0.345 to 3.269				
IC	0.917	0.313 to 2.689				
Internal medicine	1.419	0.513 to 3.929				
Lung	0.632	0.171 to 2.343				
Year 2012/2013	0.816	0.491 to 1.357	0.434			
Autopsy pathologist	1.123	0.638 to 1.977	0.688			
Brain autopsy included	0.469	0.212 to 1.036	0.061*	0.507	0.194 to 1.329	0.167

*p<0.2 were regarded as factors contributing to major discrepancies in UV analysis and included in MV analysis.
†p<0.05 were regarded as factors contributing to major discrepancies in MV analysis.
‡Departments with >20 autopsy cases were included in this analysis.
MV, multivariate; UV, univariate.

Time to completion of the autopsy report

We observed a significant reduction in the median time to the preliminary and final autopsy report from 11 days in 2007 to 3 days in 2012/2013 (p=0.001) and from 91 days in 2007 to 54 days in 2012/2013 (p<0.001), respectively. Specialised autopsy pathologists had finished their preliminary report in a median of 2 days versus general pathologists in 7 days (p=0.003), and their final report in a median of 52 days versus general pathologists in 85 days (p<0.001).

DISCUSSION

This study comparing clinical diagnoses and postmortem diagnoses demonstrates a 23.5% major discrepancy rate and a 32.6% minor discrepancy rate in 337 classifiable clinical

Table 7 Analysis of possible contributory factors to minor discrepancies between clinical and final pathology diagnosis at autopsies

	UV analysis			MV analysis		
	OR	95% CI	p Value	OR	95% CI	p Value
Age	1.012	0.993 to 1.031	0.214			
Sex	0.944	0.598 to 1.491	0.805			
Length of final admission >2 days	0.764	0.473 to 1.235	0.272			
Imaging (y/n)	0.680	0.338 to 1.369	0.370			
Active treatment discontinuation	1.991	1.233 to 3.216	0.005*	1.832	1.124 to 2.986	0.015†
Admission unit‡						
First aid	1.000		0.875			
Cardiology	0.792	0.263 to 2.385				
Surgery	1.337	0.502 to 3.560				
IC	0.968	0.378 to 2.477				
Internal medicine	1.190	0.480 to 2.947				
Lung	1.307	0.456 to 3.743				
Year 2012/2013	1.763	1.113 to 2.791	0.016*	1.608	0.987 to 2.620	0.057
Autopsy pathologist	1.532	0.924 to 2.540	0.098			
Brain autopsy included	1.326	0.737 to 2.387	0.346			

*p<0.2 were regarded as factors contributing to minor discrepancies in UV analysis and included in MV analysis.
†p<0.05 were regarded as factors contributing to minor discrepancies in MV analysis.
‡Departments with >20 autopsy cases were included in this analysis.
MV, multivariate; UV, univariate.

Table 8 The role of microscopic examination in identifying cause of death (COD) at autopsies

Role of microscopic examination	Frequency	Percentage
Provided/changed/added to COD	90	19.6
Confirmed macroscopic findings	220	47.8
No role	76	16.5
Non-classifiable	74	16.1
Total	460	100

autopsy cases. This is in line with recent literature, in which major discrepancy rates ranged from 7% to 50%, mainly depending on patient populations studied.[3 10 12–18] The 23.5% major discrepancy rate is identical to that presented in a review by Shojania *et al*[2] using the results from 42 studies.

A reason for the persistently high discrepancy rates may be selection bias because clinicians are thought to request autopsies mainly for the clinically challenging cases.[19] Nevertheless, several groups have shown that clinicians were not able to predict, based on their clinical certainty, cases that would uncover discrepant autopsy findings.[20–22] Berner and Graber[23] described clinicians' overconfidence in their diagnoses as a contributing cause of diagnostic errors. Moreover, Combes *et al*[24] demonstrated that percentages of major diagnostic discrepancies were similar between patients that had undergone modern diagnostic techniques and patients that had not, emphasising the value of the autopsy, even in the era of modern diagnostic techniques.

The most commonly observed major discrepancies found in this study were myocardial infarction, pulmonary embolism and pneumonia. This is in agreement with those found by others[25–29] and is comprehensible as myocardial infarction, pulmonary embolism and pneumonia can present atypically or even asymptomatically.[30–32] In addition, Winters *et al*[28] reported aspergillosis, which was the fifth leading major discrepancy in our study, to be a frequently missed class I disease.

Surprisingly, we found a higher percentage of major discrepancies when imaging was applied during life. Further analysis revealed that this was mainly due to imaging of an improper body part or with an improper imaging modality, thereby failing to identify the actual COD, which was the case in 15.6%.

Similar to previous studies, we demonstrated that microscopic examination has a major impact on macroscopical diagnoses made during clinical autopsies.[33–35] In our study, microscopic examination contributed to the final COD in 19.6% of cases, especially for diagnosing pneumonia, myocardial infarction and myocarditis. In accordance, Hunt *et al*[36] showed a substantial discrepancy rate between macroscopical and microscopically confirmed diagnoses of pneumonia.

In these times of fewer monetary resources, quality of care is a critical point. Identification of problematic disease categories can help to reduce the number of unnecessary deaths.[37 38] Autopsies are crucial to determine potential diagnostic errors underlying these high mortality rates and offer clinicians the opportunity to receive feedback from which lessons can be learned. Furthermore, frequent discrepant diagnoses revealed at autopsy should make healthcare organisations aware of the incidence of system-related errors and make them search for interventions on the system level, such as introducing double readings for certain diagnostic tests and offering clinical decision support opportunities.[1]

In previous studies, a longer length of admission at the ICU, of >2 days and >10 days, respectively, was significantly associated with more major discrepancies.[39 40] Contrarily, Tavora *et al*[41] found that a shorter length of hospital stay significantly contributed to major discrepant findings. Although in our study the length of final admission did not influence the frequency of major discrepancies, an admission length of >2 days significantly reduced the frequency of class III minor discrepancies. Longer admission length may influence mortality and morbidity.

Alternate non-invasive ways of postmortem examination are being explored. Virtual autopsies by means of CT and MRI have already been used in forensic medicine, and although they seemed promising in clinical medicine, there certainly are drawbacks. In several studies,[42–44] a substantial number of diagnoses were missed on virtual autopsy, and the most commonly missed ones were exactly those discrepancies most frequently described in literature as well as in our study.

Due to technical and practical limitations, routine toxicology tests were not included in our clinical autopsy protocols, in line with most other pathology labs. However, routine toxicology testing may reveal otherwise undetected CODs, including death from fatal adverse drug reactions to properly prescribed and administered drugs. These adverse drug reactions have been described to be between the fourth and sixth leading COD in the USA.[45] In future studies, we would like to analyse the value of routine toxicology testing.

In The Netherlands, relatives have to give separate permission for body and brain autopsy, leading to a relatively low number of the latter. This is another limitation of this study since intracranial pathology in cases without brain autopsy cannot be excluded. As a complete autopsy includes the brain, efforts should be made by clinicians to obtain relatives' consent. Furthermore, pathologists should make clinicians more aware of the importance of a complete autopsy.

Regarding the autopsy report, we make several recommendations, based on literature and our own experiences. The preliminary report should preferably be distributed within 24 h. It has been proven effective to start with the main findings (COD and major discrepancies) and to describe further findings point by point.[46] Immediate reporting will be most effective as clinicians can directly reflect on their diagnoses.[47] The final report should be distributed within 1 month since reports received after 1 month are much less useful to clinicians.[48] The timing of feedback is important. Immediate feedback is more effective than delayed feedback.[49] Although in our subset of cases the median time to completion of the autopsy report was longer than 1 month, we observed a significant reduction in the median time to the preliminary and final autopsy report over the study period, mainly ascribed to the deployment of specialised autopsy pathologists who are apparently more dedicated to completing the final reports.

Take home messages

- Major discrepancies between clinical and autopsy diagnoses were found in 23.5% of the clinical autopsies.
- Myocardial infarction, pulmonary embolism and pneumonia were the most commonly observed discrepancies.
- Improper imaging was significantly associated with a higher percentage of major discrepancies.
- Even in the era of high-tech medicine, the autopsy remains an important tool for quality assessment of clinical diagnoses.

CONCLUSION

Major discrepancies remain persistent at autopsy, even in the era of high-tech medicine. Therefore, they still serve as a very important part of quality control in clinical diagnosis and treatment. Learning from individual and system-related diagnostic errors can aid in improving patient safety.

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The value of autopsies in the era of high-tech medicine: discrepant findings persist

Chantal C H J Kuijpers, Judith Fronczek, Frank R W van de Goot, et al.

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